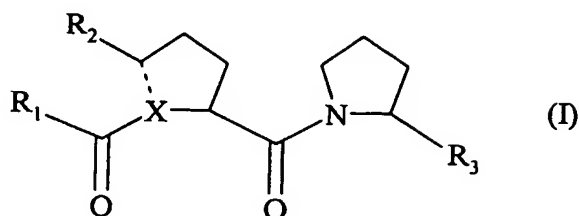


CLAIMS

1. A compound of formula (I)



5

wherein in the formula, X is N or C;

the dotted line represents a single or a double bond;

- 10 R_1 is:

a straight or branched alkyl chain having 1 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) each independently being COOR^4 , COR^4 , $\text{CR}^4(\text{OR}^5)_2$, COCH_2OR^6 , cyano, hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl
 15 lower alkoxy, nitro, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, wherein R^4 is H, lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, heterocycle, aryl or aralkyl, R^5 is lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, aryl or aralkyl and R^6 is H, lower alkyl, lower acyl or halogen,

- 20 a straight or branched alkenyl chain having 2 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group above,

a 3 to 7 membered, saturated or unsaturated, carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl
 25 group above,

a 3 to 7 membered, saturated or unsaturated, heterocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined

for the alkyl group above,

a substituted or unsubstituted alkyl or alkenyl group as defined above incorporating as a group member a substituted or unsubstituted carbocyclic ring or a heterocyclic ring as
5 defined above,

hydroxy, lower alkoxy, aryloxy, aryl lower alkoxy, amino, amino lower alkyl, lower alkyl amino, aryl amino or aryl lower alkyl amino, wherein the said alkyl, aryl or amino subgroups are unsubstituted or substituted with 1 to 3 substituent(s) each independently
10 being lower alkyl or as defined for the alkyl group above;

R_2 is:

H,
15

a straight or branched alkyl chain having 1 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) each independently being hydroxy, oxo, lower alkoxy, amino, lower alkyl amino, halogen, carboxyl or lower acyl,

20 a straight or branched alkenyl chain having 2 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group, in the meaning of R_2 , above,

or a straight or branched alkynyl chain having 2 to 10 carbon atoms unsubstituted or
25 substituted with 1 to 3 substituent(s) as defined for the alkyl group, in the meaning of R_2 , above;

R_3 is:

30 H, cyano, hydroxy, oxo, halogen, lower alkyl, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, wherein the said alkyl subgroups are unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group, in the meaning of R_1 , above,

or R_3 is COOR^4 , COR^4 , $\text{CR}^4(\text{OR}^5)_2$ or COCH_2OR^6 , wherein R^4 is H, lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, heterocycle, aryl, amino, lower alkyl amino, aryl amino or lower alkyl amino, wherein the said lower alkyl is unsubstituted or substituted with 1
5 or 2 substituent(s) each independently being cyano, hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, R^5 is lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, aryl or aralkyl and R^6 is lower acyl or halogen;

10 provided, that

a) when X is N, the dotted line represents a single bond and R_2 is not H;

b) when X is C, the dotted line represents a double bond and R_2 is H;

or a pharmaceutically acceptable salt or ester thereof.

15 2. A compound according to claim 1, wherein

X is N;

the dotted line represents a single bond;

20

R_1 is:

a straight or branched alkyl chain having 1 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) each independently being COOR^4 , COR^4 ,
25 $\text{CR}^4(\text{OR}^5)_2$, COCH_2OR^6 , cyano, hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, nitro, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, wherein R^4 is H, lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, heterocycle, aryl or aralkyl, R^5 is lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, aryl or aralkyl and R^6 is H, lower alkyl, lower acyl or halogen,

30

a straight or branched alkenyl chain having 2 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group above,

a 3 to 7 membered, saturated or unsaturated, carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,

- 5 a 3 to 7 membered, saturated or unsaturated, heterocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,

- 10 a substituted or unsubstituted alkyl or alkenyl group as defined above incorporating as a group member a substituted or unsubstituted carbocyclic ring or a heterocyclic ring as defined above,

- 15 hydroxy, lower alkoxy, aryloxy, aryl lower alkoxy, amino, amino lower alkyl, lower alkyl amino, aryl amino or aryl lower alkyl amino, wherein the said alkyl, aryl or amino subgroups are unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl group above;

R₂ is:

- 20 a straight or branched alkyl chain having 1 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) each independently being hydroxy, oxo, lower alkoxy, amino, lower alkyl amino, halogen, carboxyl or lower acyl,

- 25 a straight or branched alkenyl chain having 2 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group, in the meaning of R₂, above,

- 30 or a straight or branched alkynyl chain having 2 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group, in the meaning of R₂, above;

R₃ is:

H, cyano, hydroxy, oxo, halogen, lower alkyl, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, wherein the said alkyl subgroups are unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group, in the meaning of R₁, above,

5

or R₃ is COOR⁴, COR⁴, CR⁴(OR⁵)₂ or COCH₂OR⁶, wherein R⁴ is H, lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, heterocycle, aryl, amino, lower alkyl amino, aryl amino or lower alkyl amino, wherein the said lower alkyl is unsubstituted or substituted with 1 or 2 substituent(s) each independently being cyano, hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, R⁵ is lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, aryl or aralkyl and R⁶ is lower acyl or halogen, or a pharmaceutically acceptable salt or ester thereof.

10

15 3. A compound according to claim 2, wherein

R₁ is

a straight or branched alkyl chain having 1 to 5 carbon atoms unsubstituted or substituted with 1 or 2 substituent(s) each independently being hydroxy, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle,

20

a 3 to 7 membered, saturated or unsaturated, carbocyclic ring unsubstituted or substituted with 1 or 2 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,

25 a 3 to 7 membered, saturated or unsaturated, heterocyclic ring unsubstituted or substituted with 1 or 2 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,

a substituted or unsubstituted alkyl or alkenyl group as defined above incorporating as a group member a substituted or unsubstituted carbocyclic ring or a heterocyclic ring as defined above,

30

hydroxy, lower alkoxy, aryloxy, aryl lower alkoxy, amino, amino lower alkyl, lower alkyl amino, aryl amino or aryl lower alkyl amino, wherein the said alkyl, aryl or amino subgroups are unsubstituted or substituted with 1 to 3 substituent(s) each independently

being lower alkyl or as defined for the alkyl group above;

R₂ is

a straight or branched alkyl chain having 1 to 5 carbon atoms unsubstituted or substituted
5 with 1 or 2 substituent(s) each independently being hydroxy, oxo, lower alkoxy, amino, lower alkyl amino, halogen, carboxyl or lower acyl;

R₃ is:

H, cyano or COR⁴, wherein R⁴ is H, lower alkyl, cycloalkyl, cycloalkenyl, heterocycle or
10 aryl, wherein the said lower alkyl is unsubstituted or substituted with 1 or 2 substituent(s) each independently being hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, cycloalkyl or heterocycle.

4. A compound according to any one of claims 2 or 3, wherein
15

R₁ is

a straight alkyl chain having 1 to 3 carbon atoms unsubstituted or substituted with 1 or 2
substituent(s) each independently being aryl, aryloxy, aryl lower alkoxy, lower alkyl
amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle,
20 a 3 to 7 membered, saturated or unsaturated, unsubstituted heterocyclic ring, lower alkoxy, lower alkyl amino, aryl amino or aryl lower alkyl amino;

R₂ is a straight or branched unsubstituted alkyl chain having 1 to 4 carbon atoms;

25 R₃ is:

H, cyano or COR⁴, wherein R⁴ is H or lower alkyl, wherein the said lower alkyl is unsubstituted or substituted with hydroxy.

5. A compound according to claim 1, wherein
30

X is C;

the dotted line represents a double bond;

R₁ is:

5 a straight or branched alkyl chain having 1 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) each independently being COOR⁴, COR⁴, CR⁴(OR⁵)₂, COCH₂OR⁶, cyano, hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, nitro, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, wherein R⁴ is H, lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, heterocycle, aryl or aralkyl, R⁵ is lower alkyl, lower alkenyl, cycloalkyl, 10 cycloalkenyl, aryl or aralkyl and R⁶ is H, lower alkyl, lower acyl or halogen,

a straight or branched alkenyl chain having 2 to 10 carbon atoms unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group above,

15 a 3 to 7 membered, saturated or unsaturated, carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,

20 a 3 to 7 membered, saturated or unsaturated, heterocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,

25 a substituted or unsubstituted alkyl or alkenyl group as defined above incorporating as a group member a substituted or unsubstituted carbocyclic ring or a heterocyclic ring as defined above,

30 hydroxy, lower alkoxy, aryloxy, aryl lower alkoxy, amino, amino lower alkyl, lower alkyl amino, aryl amino or aryl lower alkyl amino, wherein the said alkyl, aryl or amino subgroups are unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl group above;

R₂ is H;

R₃ is:

H, cyano, hydroxy, oxo, halogen, lower alkyl, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or
5 heterocycle, wherein the said alkyl subgroups are unsubstituted or substituted with 1 to 3 substituent(s) as defined for the alkyl group, in the meaning of R₁, above,

or R₃ is COOR⁴, COR⁴, CR⁴(OR⁵)₂ or COCH₂OR⁶, wherein R⁴ is H, lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, heterocycle, aryl, amino, lower alkyl amino, aryl amino
10 or lower alkyl amino, wherein the said lower alkyl is unsubstituted or substituted with 1 or 2 substituent(s) each independently being cyano, hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, R⁵ is lower alkyl, lower alkenyl, cycloalkyl, cycloalkenyl, aryl or aralkyl and R⁶ is lower acyl or halogen, or a pharmaceutically
15 acceptable salt or ester thereof.

6. A compound according to claim 5, wherein

R₁ is
20 a straight or branched alkyl chain having 1 to 5 carbon atoms unsubstituted or substituted with 1 or 2 substituent(s) each independently being hydroxy, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, amino, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle,
a 3 to 7 membered, saturated or unsaturated, carbocyclic ring unsubstituted or substituted
25 with 1 or 2 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,
a 3 to 7 membered, saturated or unsaturated, heterocyclic ring unsubstituted or substituted with 1 or 2 substituent(s) each independently being lower alkyl or as defined for the alkyl group above,
30 a substituted or unsubstituted alkyl or alkenyl group as defined above incorporating as a group member a substituted or unsubstituted carbocyclic ring or a heterocyclic ring as defined above,
hydroxy, lower alkoxy, aryloxy, aryl lower alkoxy, amino, amino lower alkyl, lower alkyl

amino, aryl amino or aryl lower alkyl amino, wherein the said alkyl, aryl or amino subgroups are unsubstituted or substituted with 1 to 3 substituent(s) each independently being lower alkyl or as defined for the alkyl group above;

5 R₃ is:

H, cyano or COR⁴, wherein R⁴ is H, lower alkyl, cycloalkyl, cycloalkenyl, heterocycle or aryl, wherein the said lower alkyl is unsubstituted or substituted with 1 or 2 substituent(s) each independently being hydroxy, oxo, halogen, lower alkoxy, aryl, aryloxy, aryl lower alkoxy, cycloalkyl or heterocycle.

10

7. A compound according to any one of claims 5 or 6, wherein

R₁ is

15 a straight or branched alkyl chain having 1 to 3 carbon atoms unsubstituted or substituted with 1 or 2 substituent(s) each independently being, aryl, aryloxy, aryl lower alkoxy, lower alkyl amino, aryl amino, aryl lower alkyl amino, cycloalkyl or heterocycle, a 3 to 7 membered, saturated or unsaturated, unsubstituted heterocyclic ring, lower alkoxy, amino lower alkyl, lower alkyl amino, aryl amino or aryl lower alkyl amino, wherein the amino subgroups are unsubstituted or substituted with lower alkyl;

20

R₃ is:

H, cyano or COR⁴, wherein R⁴ is H or lower alkyl, wherein the said lower alkyl is unsubstituted or substituted with hydroxy.

25 8. A pharmaceutical composition comprising at least one compound of formula (I) according to any one of claims 1 to 7 and a pharmaceutically acceptable diluent, carrier and/or excipient.

30 9. A compound of formula (I) according to any one of claims 1 to 7 for use as a prolyl oligopeptidase inhibitor.

10. The use of a compound of formula (I) or a pharmaceutically acceptable ester or salt thereof according to any one of claims 1 to 7 for the manufacture of a medicament for

use as a prolyl oligopeptidase inhibitor.

11. The use of a compound of formula (I) according to any one of claims 1 to 7 for
the manufacture of a medicament for the treatment of neurodegenerative diseases, and/or
5 for the improvement of learning and memory functions.
12. The use according to claim 11, wherein the neurodegenerative disease is
Alzheimer's disease or senile dementia.
- 10 13. A method for the treatment of a disease or the enhancement of a condition where
prolyl oligopeptidase inhibitors are indicated to be useful, which comprises administering
to a subject in need of the treatment an effective amount of at least one compound of
formula (I) according to claim 1.
- 15 14. The method according to claim 13, which comprises treating a neurodegenerative
disease, and/or improving learning and memory functions.
15. The method according to claim 14, wherein the neurodegenerative disease is
Alzheimer's disease or senile dementia.